



TITLE:

<Division of Synthetic Chemistry>Synthetic Organic Chemistry

AUTHOR(S):

CITATION:

<Division of Synthetic Chemistry>Synthetic Organic Chemistry. ICR Annual Report 2012, 19: 8-9

ISSUE DATE:

2012

URL:

<http://hdl.handle.net/2433/172599>

RIGHT:

Division of Synthetic Chemistry – Synthetic Organic Chemistry –

<http://www.fos.kuicr.kyoto-u.ac.jp/EnglishTop/English.top.html>



Prof
KAWABATA, Takeo
(D Pharm Sc)



Assoc Prof
FURUTA, Takumi
(D Pharm Sc)



Assist Prof
YOSHIMURA, Tomoyuki
(D Pharm Sc)



Techn Staff
FUJIHASHI, Akiko



PD
MENDU, Narender
(Ph D)



PD
BHATRAJU,
Vasantha Lakshmi
(Ph D)

Students

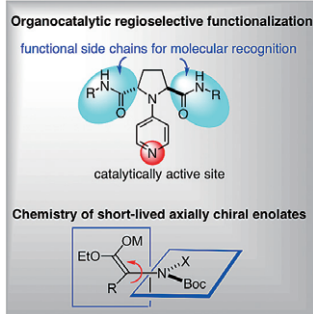
NISHINO, Reiko (D3)
UEDA, Yoshihiro (D3)
HAMADA, Shohei (D3)
MISHIRO, Kenji (D3)
KINOSHITA, Tomohiko (D2)
SHIGETA, Takashi (D1)
BABA, Tomoaki (D1)

YANAGI, Masanori (D1)
YANG, Pan (D1)
TAKEUCHI, Hironori (M2)
SHAN, Tisheng (M2)
TSUDA, Ayumi (M2)
HYAKUTAKE, Ryuichi (M2)

HIRATA, Atsushi (M2)
KASAMATSU, Koji (M1)
KURIBAYASHI, Toshifumi (M1)
HAYASAKA, Manami (M1)
OTSUKI, Haruka (UG)
WADA, Yoshiyuki (UG)

Scope of Research

The research interests of the laboratory include the development of advanced molecular transformation, total synthesis of biologically active products, and molecular recognition. Programs are active in the areas of asymmetric alkylation of carbonyl compounds based on “memory of chirality”, organocatalysis for fine organic syntheses, synthesis of unusual amino acids and nitrogen heterocycles, regioselective functionalization of carbohydrates, and the structural and functional investigation of heterochiral oligomers.



KEYWORDS

Organocatalysis
Regioselective Functionalization
Dynamic Chirality
Unusual Amino Acid
Molecular Recognition



Selected Publications

- Kawabata, T.; Matsuda, S.; Kawakami, S.; Monguchi, D.; Moriyama, K., Stereochemical Diversity in Asymmetric Cyclization via Memory of Chirality, *J. Am. Chem. Soc.*, **128**, 15394-15395 (2006).
- Kawabata, T.; Muramatsu, W.; Nishio, T.; Shibata, T.; Schedel, H., A Catalytic One-Step Process for the Chemo- and Regioselective Acylation of Monosaccharides, *J. Am. Chem. Soc.*, **129**, 12890-12895 (2007).
- Kawabata, T.; Moriyama, K.; Kawakami, S.; Tsubaki, K., Powdered KOH in DMSO: An Efficient Base for Asymmetric Cyclization via Memory of Chirality at Ambient Temperature, *J. Am. Chem. Soc.*, **130**, 4153-4157 (2008).
- Kawabata, T.; Jiang, C.; Hayashi, K.; Tsubaki, K.; Yoshimura, T.; Majumdar, S.; Sasamori, T.; Tokitoh, N., Axially Chiral Binaphthyl Surrogates with an Inner N-H-N Hydrogen Bond, *J. Am. Chem. Soc.*, **131**, 54-55 (2009).
- Yoshida, K.; Furuta, T.; Kawabata, T., Organocatalytic Chemoselective Monoacylation of 1,n-Linear Diol, *Angew. Chem. Int. Ed.*, **50**, 4888-4892 (2011).
- Yoshida, K.; Mishiro, K.; Ueda, Y.; Shigeta, T.; Furuta, T.; Kawabata, T., Nonenzymatic Geometry-Selective Acylation of Tri- and Tetrasubstituted α,α' -Alkenediols, *Adv. Syn. Catal.*, **354**, 3291-3298 (2012).
- Yoshimura, T.; Takuwa, M.; Tomohara, K.; Uyama, M.; Hayashi, K.; Yang, P.; Hyakutake, R.; Sasamori, T.; Tokitoh, N.; Kawabata, T., Protonation-Assisted Conjugate Addition of Axially Chiral Enolates: Asymmetric Synthesis of Multisubstituted β -Lactams from α -Amino Acids, *Chem. Eur. J.*, **18**, 15330-15336 (2012).

The First Example of Nonenzymatic Geometry-Selective Acylation of Tetrasubstituted α,α' -Alkenediols

Selective functionalization of hydroxy groups in polyol substrates is important in organic transformation. Differentiation of hydroxy groups of unsymmetrically substituted 2-alkylidene-1,3-propanediols has been expected to be difficult due to the similar intrinsic reactivity of the two primary hydroxy groups. In accordance with the expectation, nonenzymatic methods for geometry-selective acylation of unsymmetrically *trisubstituted* 2-alkylidene-1,3-propanediols has never been reported, while highly selective enzymatic acylation of the diols and deacylation of the corresponding diesters have been reported. However, no methods including enzymatic protocols for the *differentiation of primary hydroxy groups of tetrasubstituted 2-alkylidene-1,3-propanediols* have been reported. Here we report the first example of the highly geometry-selective acylation of tetrasubstituted 2-alkylidene-1,3-propanediols promoted by artificial catalysts. Highly *E*-selective acylation of various tetrasubstituted 2-alkylidene-1,3-propanediols was achieved in 96~>99 % selectivity by treatment of the diol substrates with acetic anhydride in the presence of 10 mol% of organocatalyst **1**.

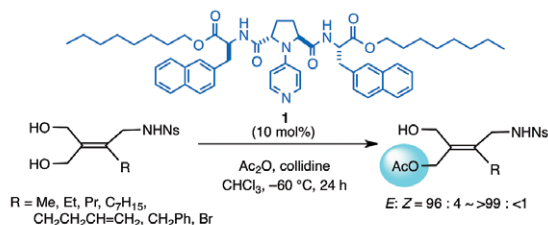


Figure 1. Geometry-selective acylation of tetrasubstituted α,α' -alkenediols promoted by organocatalyst **1**.

A Catalytic One-Step Method for Regioselective Manipulation of Biologically Active Complex Natural Products

Chemo- and regioselective manipulation of one of the multiple hydroxy groups of polyol natural products has been a fundamental challenge in organic synthesis. We describe here a regiochemical profile of acylation of a complex polyol natural product possessing eight free hydroxy groups, lanatoside C (**2**), a clinically used cardiac glycoside, which is composed of a tetrasaccharide containing a terminal glucopyranoside and an aglycon named digoxigenin. The acylation of **2** was examined with catalyst **3** and DMAP. In the presence of 10 mol% of **3**, acylation took place predominantly at C(4''')-OH in 90% regioselectivity and 87% yield for monoacylation on treatment of **2** with isobutyric anhydride in CHCl_3 -THF (9:1)

at $-60\text{ }^\circ\text{C}$. On the other hand, DMAP catalyzed acylation of **2** gave the C(3''')-*O*-acylate in up to 97% regioselectivity. Thus, diverse regioselective introduction of acyl groups among eight free hydroxy groups of lanatoside C was achieved. Various functionalized acyl groups were also regioselectively introduced at C(4''')-OH by employing an mixed anhydride method in the presence of catalyst **3** and the related organocatalyst.

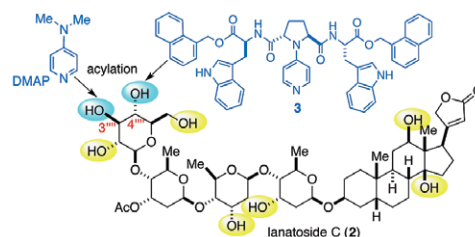


Figure 2. One-step regioselective introduction of acyl groups into lanatoside C (**2**) by organocatalysis.

Asymmetric Aldol Reaction via Memory of Chirality

Asymmetric aldol reaction of α -amino acid derivatives via memory of chirality has been developed. Although asymmetric aldol reactions have extensively developed, the present method has unique characteristics in which asymmetric induction is controlled solely by the enolate chirality in the absence of chiral catalysts or chiral auxiliaries. The reaction was assumed to proceed via axially chiral enolate intermediate **A** to give the chiral aldolate in inversion of the configuration at the newly formed tetrasubstituted carbon center. Chiral oxazolidones were obtained by intramolecular acylation of the aldolate. Thus, chiral oxazolidone derivatives with contiguous tetra- and trisubstituted chiral centers were readily obtained from abundant α -amino acids in a highly diastereoselective and enantioselective manner. Chiral oxazolidones have been known to be useful chiral auxiliaries in organic synthesis, and recently disclosed to be a novel class of antibiotics. Oxazolidones obtained by the present method are the structural equivalent to β -hydroxy- α -amino acids with a tetrasubstituted carbon center, which are the frequently observed structural subunits in biologically active natural products.

